

AMENDMENTS TO THE CLAIMS

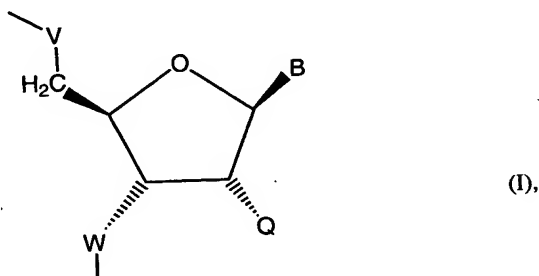
In the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Withdrawn) An oligonucleotide derivative which is specifically hybridizable to a region ranging from base position no. 687 (5') to no. 706 (3') of the human bcl-xL mRNA encoding human bcl-xL protein.
2. (Currently Amended) An The oligonucleotide derivative which is specifically hybridizable to a region ranging from base position no. 687 (5') to no. 706 (3') of the human bcl-xL mRNA encoding human bcl-xL protein according to claim 1, which oligonucleotide derivative additionally is specifically hybridizable to a region ranging from base position 2032 (5') to 2051 (3') of the human bcl-2 mRNA encoding human bcl- protein.
3. (Currently Amended) The oligonucleotide derivative according to claim ~~1~~ 2 comprising a base sequence which is complementary to at least a part of the said region of the human bcl-xL mRNA or the human bcl-2 mRNA, or wherein such base sequence contains up to 3 mispairing building blocks, or wherein such base sequence contains up to 3 abasic building blocks.
4. (Currently Amended) The oligonucleotide derivative according to claim ~~1~~ 2 having a length of 8 to 25 consecutive building blocks.
5. (Original) The oligonucleotide derivative according to claim 4 having a length of 20 consecutive building blocks.
6. (Previously Amended) The oligonucleotide derivative according to claim 3, wherein said base sequence is selected from the group consisting of the base sequence 5'-AAGGCATCCCAGCCTCCGTT-3' (SEQ ID NO: 3), the base sequence 5'-AAAGTATCCCAGCCGCCGTT-3' (SEQ ID NO: 4), and the base sequence 5'-AAAGCATCCCAGCCTCCGTT-3' (SEQ ID NO: 5).
7. (Currently Amended) The oligonucleotide derivative according to claim ~~1~~ 2, consisting of a base sequence selected from the group consisting of the base sequence 5'-AAGGCATCCCAGCCTCCGTT-3' (SEQ ID NO: 3), the base sequence 5'-

AAAGTATCCCAGCCGCGTT-3' (SEQ ID NO: 4) and the base sequence 5'-AAAGCATCCCAGCCTCCGTT-3' (SEQ ID NO: 5).

8. (Currently Amended) The oligonucleotide derivative according to claim 2, comprising at least one building block of formula (I)



wherein

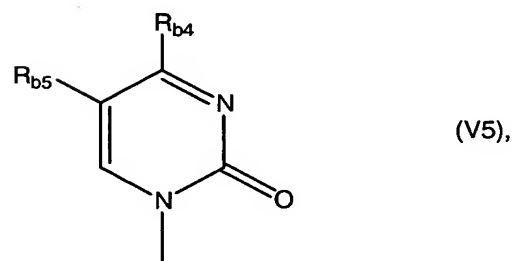
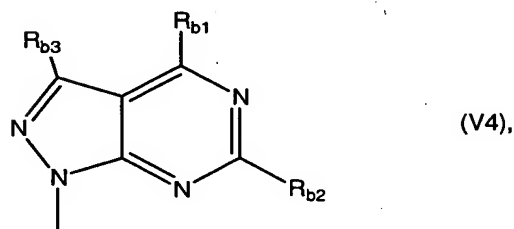
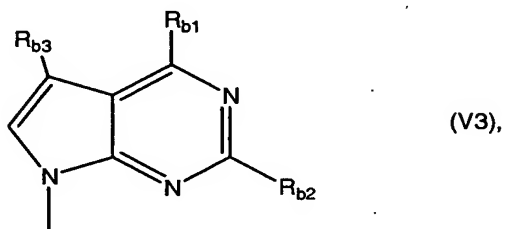
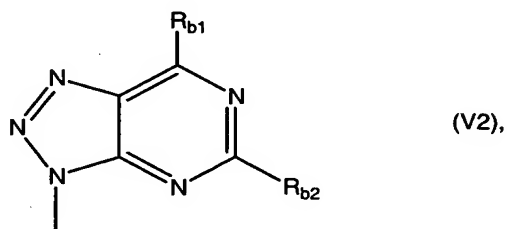
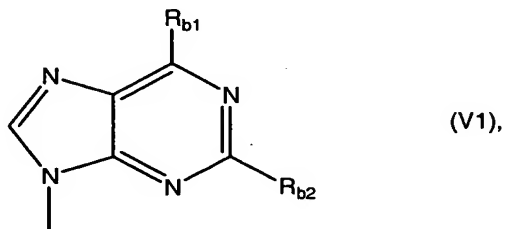
Q is H, -OCH₃, -O(CH₂CH₂)_nOCH₃, or -OCH₂CH₂NR₁R₂, wherein R₁ and R₂ are, independently of each other, H or -CH₃, and wherein n is 1, 2 or 3;

V and W are, independently of each other, the same or different radicals of an internucleosidic bridging group selected from the following group: 5'-O-P(O)(OH)-O-3' (phosphodiester), 5'-O-P(O)(SH)-O-3' (phosphorothioate), 5'-O-P(S)(SH)-O-3' (phosphodithioate), 5'-O-P(O)(CH₃)-O-3' (methylphosphonate), 5'-O-P(O)(NH-R₇)-O-3' (phosphoamidate) in which R₇ is C₁-C₃ alkyl, 5'-O-P(O)(OR₈)-O-3' (phosphotriester) in which R₈ is C₁-C₃ alkyl, 5'-O-S(O)₂-CH₂-3' (sulfonate), 5'-O-S(O)₂-NH-3' (sulfamate), 5'-NH; S(O)₂-CH₂-3' (sulfonamide), 5'-CH₂-S(O)₂-CH₂-3' (sulfone), 5'-O-S(O)-O-3' (sulfite), 5'-CH₂-S(O)-CH₂-3' (sulfoxide), 5'-CH₂-S-CH₂-3' (sulfide), 5'-O-CH₂-O-3' (formacetal), 5'-S-CH₂-O-3' (3'-thioformacetal), -CH₂-S-3' (5'-thioformacetal), 5'-CH₂-CH₂-S-3' (thioether), 5'-CH₂-NH-O-3' (hydroxylamine), 5'-CH₂-N(CH₃)-O-3' (methylene (methylimino)), 5'-CH₂-O-N(CH₃)-3' (methyleneoxy (methylimino)), 5'-O-C(O)-NH-3' (5'-N-carbamate), 5'-CH₂-C(O)-NH-3' (amide), 5'-NH-C(O)-CH₂-3' (amide 2), 5'-CH₂-NH-C(O)-3' (amide 3) and 5'-C(O)-NH-CH₂-3' (amide 4), and the tautomeric forms thereof;

or one of V and W is such an internucleosidic bridging group and the other is a terminal radical selected from the group consisting of -OH and -NH₂, preferably -OH; and

B is a radical of a nucleic acid base; with the proviso that if Q is H, then at least one of V or W is an internucleosidic bridging group other than 5'-O-P(O)(OH)-O-3' (phosphodiester).

9. (Original) An oligonucleotide derivative according to claim 8, wherein B is a radical of the formula (V1), (V2), (V3), (V4) or (V5)



in which

R_{b1} is -NH₂, -SH or -OH;

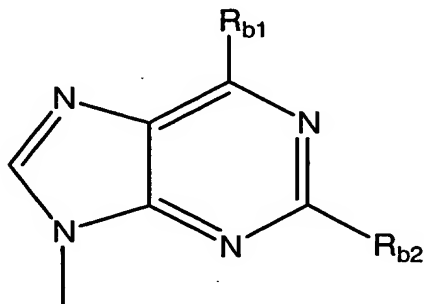
R_{b2} is H, -NH₂ or -OH; and

R_{b3} is H, Br, I, -CN, $-C\equiv C-CH_3$, $-C(O)NH_2$ or $-CH_3$;

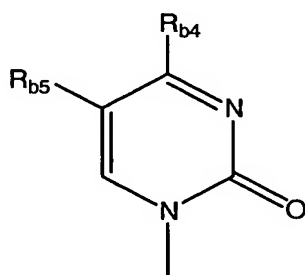
R_{b4} is $-NH_2$ or $-OH$; and

R_{b5} is H, F, Br, I, -CN, $-C\equiv C-CH_3$, $-C(O)NH_2$ or $-CH_3$.

10. (Original) An oligonucleotide derivative according to claim 9, wherein B is a radical of the formula (V1) or (V5)



(V1),



(V5),

in which

R_{b1} is $-NH_2$, $-SH$ or $-OH$;

R_{b2} is H, $-NH_2$ or $-OH$;

R_{b4} is $-NH_2$ or $-OH$; and

R_{b5} is H, F, Br, I, CN, $-C\equiv C-CH_3$, $C(O)NH_2$ or $-CH_3$.

11. (Original) An oligonucleotide derivative according to claim 10, wherein B is selected from the group of the following radicals: xanthine, hypoxanthine, adenine, 2-aminoadenine, guanine, 6-thioguanine, uracil, thymine, cytosine, 5-methylcytosine, 5-propynyluracil, 5-fluorouracil and 5-propynylcytosine.

12. (Original) An oligonucleotide derivative according to claim 8, wherein V and W, as radicals of an internucleosidic bridging group, are, independently of each other,

selected from the following group: 5'-O-P(O)(OH)-O-3' (phosphodiester), 5'-O-P(O)(SH)-O-3' (phosphorothioate) and 5'-CH₂-C(O)-NH-3' (amide).

13. (Original) An oligonucleotide derivative according to claim 12, wherein one of the radicals V or W, as radicals of an internucleosidic bridging group, is 5'-O-P(O)(OH)-O-3' (phosphodiester) and the other radical is 5'-O-P(O)(SH)-O-3' (phosphorothioate).

14. (Original) The oligonucleotide derivative according to claim 13, wherein both V and W as radicals of an internucleosidic bridging group are 5'-O-P(O)(OH)-O-3' (phosphodiester) or are 5'-O-P(O)(SH)-O-3' (phosphorothioate).

15. (Original) The oligonucleotide derivative according to claim 8, wherein V and W, as terminal radicals, are, independently of each other, -OH or -NH₂.

16. (Original) The oligonucleotide derivative according to claim 8, wherein Q is selected from the group consisting of 2'-O-methyl, 2'-O-methoxyethoxy, 2'-O-di(methoxyethoxy), 2'-O-tri(methoxyethoxy), 2'-O-aminoethoxy, 2'-O-monomethylaminoethoxy and 2'-O-dimethylaminoethoxy.

17. (Original) The oligonucleotide derivative according to claim 8, consisting of a base sequence selected from the group consisting of the base sequence 5'-AAGGCATCCCAGCCTCCGTT-3' (SEQ ID NO: 3) and the base sequence 5'-AAAGTATCCCAGCCGCCGTT-3' (SEQ ID NO: 4), wherein each V and each W as radicals of an internucleosidic bridging group of the building blocks according to formula(I) are of the 5'-O-P(O)(SH)-O-3' (phosphorothioate) type and wherein each Q according to formula(I) is -H.

18. (Original) The oligonucleotide derivative according to claim 8, consisting of a base sequence selected from the group consisting of the base sequence 5'-AAGGCATCCCAGCCTCCGTT-3' (SEQ ID NO: 3), the base sequence 5'-AAAGTATCCCAGCCGCCGTT-3' (SEQ ID NO: 4), and the base sequence 5'-AAAGCATCCCAGCCTCCGTT-3' (SEQ ID NO: 5), wherein each V and each W as radicals of an internucleosidic bridging group of all building blocks according to formula (I) are of the 5'-O-P(O)(SH)-O-3' (phosphorothioate) type, and wherein each Q according to formula (I) of

the nucleotides being underlined is $-OCH_2CH_2OCH_3$ and wherein each Q according to formula(I) of the remaining nucleotides is -H.

19. (Withdrawn) A process for the preparation of an oligonucleotide derivative according to claims 1, said process comprising incorporating at least one building block of formula (I) according to claim 8 into the oligonucleotide derivative during oligonucleotide synthesis.

20. (Withdrawn) A pharmaceutical composition comprising an oligonucleotide derivative according to claim 1, optionally together with a pharmaceutically acceptable excipient and/or auxilliary substance, said pharmaceutical composition being suitable for administration to humans suffering from a disease that responds to the modulation of human bcl-xL expression or that responds to the modulation of human bcl-xl and human bcl-2 expression.

21. (Withdrawn) An oligonucleotide derivative according to claim 1 for use in medicine.

22. (Withdrawn) Use of an oligonucleotide derivative according to claim 1 in the preparation of a pharmaceutical composition for treatment of a disease status associated with the biosynthesis of human bcl-xL protein or with the biosynthesis of both the human bcl-xL protein and the human bcl-2 protein.

23. (Withdrawn) A method of treatment of a disease status associated with the expression of human bcl-xL protein or with the expression of both the human bcl-xL protein and the human bcl-2 protein, comprising application of an oligonucleotide derivative according to claim 1.

24. (Withdrawn) A method of modulating the biosynthesis of human bcl-xL protein in a cell, comprising application of an oligonucleotide derivative according to claim 1 to said cell.

25. (Withdrawn) An oligonucleotide derivative according to claim 1 for use in a diagnostic method.

26. (Currently Amended) A pharmaceutical composition comprising an oligonucleotide derivative according to claim 1 ± 2.